Remarks

Claims 8, 10 and 24 are amended and claims 31-33 and 36-37 are cancelled; as a result, claims 8, 10-12 and 23-24, 27, 29-30 and 34-35 are currently pending.

Claim 8 has been amended to clarify that the recited specimen comprises both a blood substitute interferent and a non-blood substitute interferent.

Claim 10 has been amended to replace the term "chosen" with the term —selected—, for consistency with proper Markush language. Claim 10 has also been amended to correct a spelling error in the term "consisting".

Claim 24 has been amended to indicate that the specimen contains a blood substitute interferent.

The 35 U.S.C. § 103 Rejections

The Examiner rejected claims 8, 10-12, 23-24, 27 and 29-37 under 35 U.S.C. § 103(a) as being unpatentable over Davis in view of Sagusa, Gimpel, Simon and Christenson, Leissing or Mullins. More particularly, the Examiner has alleged that it would have been obvious to one of ordinary skill in the art at the time the invention was made to include substances such as blood substitutes disclosed by Christenson, Leissing or Mullins as interfering substances into the correction method of Davis.

Claims 31-33 and 36-37 have been cancelled without prejudice or disclaimer. The Examiner's rejection of these claims has, therefore, been rendered moot.

Applicant respectfully traverses the Examiner's rejection against claims 8, 10-12, 23-24, 27, 29-30 and 34-35 for the reasons set forth below.

Three criteria must be met in order to establish a *prima facie* case of obviousness. First, there must be some suggestion or motivation in the references or in the knowledge generally available to one of ordinary skill in the art to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. M.P.E.P. § 2142.

Davis discloses a method of estimating a change in the concentration of an analyte in a whole-blood sample, which is due to the hemolysis of red blood cells,

comprising separating a plasma fraction from the whole blood sample, estimating the quantity of extracellular hemoglobin in the plasma fraction, estimating a change in the analyte concentration in the sample due to the hemolysis of whole blood cells, and adjusting the apparent concentration of the analyte to account for the proportion of same which is due to the hemolysis of red blood cells (column 6, lines 3-16; column 8, lines 40-56).

Davis suggests that the amount of hemoglobin in the plasma sample may be determined by measuring the reflectance of the sample using a wavelength at which hemoglobin exhibits a maximum absorbance, and by using a graph of reflectance vs. hemoglobin concentration, derived from a set of samples containing known amounts of hemoglobin, to determine the concentration of hemoglobin in the plasma sample (column 8, lines 18-21 and 28-36).

Neither Davis, nor any one of the other cited references, teaches or suggests a method for determining the concentration of an analyte in a specimen comprising a blood substitute interferent, as recited in present claim 8. In particular, Davis does not teach or suggest the instantly claimed method of determining a corrected concentration of an analyte in a specimen comprising both a blood substitute interferent and a non-blood substitute interferent, which includes a step of removing the contribution of both a blood substitute interferent and a non-blood substitute interferent from an initially measured concentration of the analyte, to produce the corrected concentration of the analyte.

Furthermore, neither Davis, nor any of the other cited references, discloses the method as presently recited in claim 24, which involves determining the presence of true hemolysis in a specimen containing a blood substitute interferent.

In addition, neither Davis, nor any one of the other cited references, teaches or suggests a method that involves the use of one or more than one calibration algorithm developed using a calibration set comprising variable amounts of a blood substitute interferent and a non-blood substitute interferent, for use in a method of correcting the concentration of an analyte in a specimen, as recited in claim 8, or for use in a method of determining the presence of true hemolysis in a specimen containing a blood

substitute interferent, as recited in claim 24. Thus, whether taken alone or combined, the cited references do not disclose or suggest all the elements of any of the claims.

Furthermore, the combination of the cited references provides no suggestion or motivation to modify the disclosure of Davis to arrive at the invention of claims 8, 10-12, 23-24, 27, 29-30 and 34-35. The cited documents also provide no reasonable expectation of success at practicing a method for determining a corrected concentration of an analyte in a specimen comprising a blood substitute interferent and a non-blood substitute intereferent, where the method involves measuring an absorbance or reflectance of radiation of the specimen, wherein the measuring is performed in the absence of any reaction step that generates a chromophore within the specimen or a method of determining the presence of true hemolysis in a specimen containing a blood substitute interferent. Thus, the cited references fail to provide any of the three requirements for a *prima facie* case of obviousness over claims 8, 10-12, 23-24, 27, 29-30 and 34-35.

Applicant also provides the following comments regarding the other references cited by Examiner:

Christenson et al. disclose that hemoglobin based blood substitutes interfere with routine chemical tests, and the dilution of the sample is suggested as a way to avoid interference. There is no teaching or suggestion in Christenson et al. as to how an interferent may be identified and/or quantified in a blood sample comprising a blood substitute. Applicant, therefore, respectfully submits that Christenson et al. help define the problem in the art that the present invention is solving, that being, determining the concentration of an interferent in a sample, and if desired, correcting for the concentration of the interferent when establishing the concentration of an analyte in the sample.

Leissing et al. disclose modifications of clinical chemistry methods to overcome interferences from diaspirin crosslinked haemoglobin (DCLHb). The abstract discloses that filtering samples through an Amicon Centrifree micropartition system can remove concentrations of DCLHb up to 5000 mg/dl, producing a filtrate with molecular weight constituents less than 30000 daltons. Furthermore, for the

detection of some analytes, dilution of the sample is required, in a method similar to that disclosed in Christenson. Leissing et al. do not disclose or suggest the subject matter that is disclosed by the claims of the instant application. Leissing, as noted for Christenson, define the problem in the art that the present invention is solving.

Mullins et al. disclose that fluosol may lead to potential errors in the analysis of blood specimens. There is no disclosure or suggestion as to how an interferent may be identified and/or quantified in a blood sample that comprises a blood substitute. Rather, Mullins et al. further define the problem that the present invention is addressed to solving.

As Davis does not disclose or suggest that its method could be used with samples containing blood substitute interferents, such as those disclosed in Christenson et al., Leissing et al., or Mullins et al., one skilled in the art would not, therefore, be motivated to combine the teachings of Davis with Christenson et al., Leissing et al., or Mullins et al. to arrive at the method of claims 8, 10-12, 23-24, 27, 29-30 or 34-35 of the present application.

The Examiner also alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use different wavelengths as disclosed in Sagusa to differentiate between true hemolysis and plasma discoloration due to circulating colored substances as disclosed by Simon in the Davis method. Applicant respectfully disagrees.

The Sagusa patent discloses a colorimetric method for measuring components in a sample in the presence of interfering chromogens. In the method disclosed in the Sagusa patent, a color former is added to blood samples for colouring, and measurements for specific components are determined based on the light absorbance caused by the colouring. The measurements for specific components are corrected by the degree of chyle, degree of hemolysis and degree of icterus, which are determined at different wavelengths.

Simon et al. disclose that iron dextran therapy may cause a red-brown discolouration of the plasma simulating a hemolytic transfusion reaction. The

method used in Simon et al. to detect the iron, comprises adding Gomori's iron stain (page 342, last paragraph, left hand column) and obtaining a blue colour.

There is no teaching or suggestion in Sagusa or Simon et al. of a method of determining the concentration or presence of an analyte contained in a specimen using the method as defined in claim 8 and 24, respectively, as no exogenous reagent is added to the sample in the methods defined in the claims of the present application. It is, therefore, respectfully asserted that even if the calibration algorithms of claims 8 and 24 are construed as being algorithms developed using analyses of absorbance or reflectance over a plurality of wavelengths, the methods defined by the present claims do not involve a step of converting an analyte to a chromophore, as required by the method of Sagusa or Simon et al. Furthermore, neither Sagusa nor Simon et al. disclose a correction method using a calibration algorithm developed using a calibration set including a blood substitute interferent, and a non-blood substitute interferent, such as hemoglobin. One skilled in the art would not, therefore, be motivated to combine the teachings of Sagusa and Simon et al. with that of Davis, and one, or more of Christenson et al., Leissing et al. or Mullins et al. to arrive at the presently claimed invention.

The Examiner also alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a derivative spectroscopic method as shown by Gimpel for correction in the Davis method. Applicant respectfully disagrees.

Gimpel et al. disclose a method of measuring total bilirubin concentrations in cerebrospinal fluid by using derivative spectroscopy and the formation of azobilirubin derivatives. Gimpel et al. does not, however, provide any teaching or suggestion of a method for determining the concentration of bilirubin without using azobilirubin derivatives.

It is respectfully asserted that even if the calibration algorithms of claims 8 and 24 are construed as being algorithms developed using derivative analyses of spectra, the methods defined by the present claims do not involve a step of converting an analyte to a chromophore, as required by the method of Gimpel et al. One skilled

in the art would not, therefore, be motivated to combine the teaching of Gimpel et al. with that of Davis, and one, or more of Christenson et al., Leissing et al. or Mullins et al. to arrive at the presently claimed invention.

Applicant, therefore, submits that Davis, in combination with Christenson et al., Leissing et al. or Mullins et al., and any of the other cited references do not teach or suggest the method of determining the concentration or presence of an analyte in a specimen containing a blood substitute interferent, as claimed in claims 8 and 24, respectively.

Therefore, the Examiner is respectfully requested to withdraw the rejection of claims 8, 10-12, 23-24, 27 and 29-37 under Section 35 U.S.C. § 103(a).

Conclusion

All of the stated grounds of objection and rejection have been properly traversed or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all of the outstanding objections and rejections, and allow all pending claims.

It is believed that a full and complete reply has been made to the outstanding Office Action, and as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned attorney at the number provided.

Prompt consideration of the forgoing amendments and remarks, and allowance of all pending claims, are earnestly solicited.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

JAMES SAMSOONDAR ET AL.

By their Representatives,
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6905

Date NOV. 15, 2004

By _____
Monique M. Perdok Shonka
Reg. No. 42,989

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 15 day of November, 2004.

PATRICIA A. HULTMAN

Name

Signature